

Attorney Docket: Beirsdorf 602

**CONDITIONAL PETITION FOR EXTENSION OF TIME**

If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge the required fee to Deposit Account No. 14-1263.

**ADDITIONAL FEES**

Please charge any further insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

**REMARKS**

All previous claims are canceled, and new claims 30-50 have been added.

The undersigned gratefully acknowledges the withdrawal of the finality of the previous office action. The issues raised in the numbered paragraphs of the office action are addressed by the amendments to the claims taken together with the ensuing comments.

Favorable consideration of the amended claims is respectfully requested.

**Paragraph 1**

The objection to claim 21 is mooted by cancellation of the claim.

**Paragraphs 2-3**

The rejection of claims 21-29 is rendered moot by the claims' cancellation.

**Paragraphs 4-5**

The rejection of claims 25-26 is rendered moot by the claims' cancellation.

**Paragraph 6**

The rejection of claims 23-24 is rendered moot by the claims' cancellation.

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Paragraphs 7-9

A. The claims are rejected over Fortier in view of Galin. The crux of the rejection is that Fortier teaches crosslinking of catalase to PEG hydrogels, wherein the presence of albumin during preparation of the crosslinked hydrogel is viewed by Examiner as being optional.

In support of this interpretation, Examiner cites Fortier, col. 14.

However, the cited text indicates that Fortier's hydrogel prepared in the absence of albumin dissolved. Thus, Fortier's albumin-free hydrogel is not only inoperative, it apparently ceased to exist as a functional structurally intact hydrogel.

In view of this, it is unclear why Examiner believes that Fortier's results would provide to persons in the art, a reasonable expectation of success in developing the claimed hydrogel based on Fortier's teachings.

Further, Fortier explicitly and unambiguously states that his data "clearly demonstrates the unexpected important role of albumin protein in maintaining the integrity of the hydrogel structure. Consequently, albumin plays a key role as a co-protein of reticulation." Lines 60-64.

In view of Fortier's explicit disclosure of the requirement for albumin in preparing his hydrogel, it is not reasonable to conclude that albumin is *merely an optional* component. By ignoring Fortier's own interpretation of his own results, Examiner seems committed to maintaining the rejections based on her own view of Fortier's teachings, even if such a view is not supported by the disclosure. It is indisputable that without albumin, Fortier cannot provide a functional and intact hydrogel. Any interpretation of the references along the lines that Fortier's hydrogel may be optionally prepared in the absence of albumin is factually incorrect and therefore, legally insufficient to maintain the rejection.

Fortier's disclosure would indisputably provide persons in the art with an expectation that protein-PEG hydrogels would require albumin for functionality and structural integrity. The Applicants' hydrogel lacks this requirement. According to PTO guidelines and the BPAI, this absence of an albumin requirement is evidence of unobviousness. § MPEP 716.02(a).

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For this reason alone, the rejection should be withdrawn as Galin does not cure the defects in Fortier, as described below in section B.

B. Galin only shows that PEG and a diisocyanate can be reacted to form a crystalline body. Examiner has also indicated that this is her only reason for citing Galin. Office action, page 9, 3rd paragraph.

Galin combined with Fortier, does not provide persons of ordinary skill in the art a reasonable expectation of success that substituting Galin's modified PEGs in place of Fortier's PEGs, would yield a hydrogel with properties similar to that of the claimed subject matter.

What is key in the claimed hydrogel is that the Applicants have shown that their activated PEG provides a hydrogel that does not require albumin to prevent dissolution of the matrix.

There is absolutely nothing in Fortier or Galin to render the claimed hydrogel's superior properties reasonably predictable. Therefore, the Fortier and Galin are not sufficient to render the claims obvious. MPEP § 2143.02. Examiner's comments seem to center that the actual substitution is physically within the capabilities of skilled artisans, but it is long held that this is not sufficient to render the claims obvious. "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2143.02, citing *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990).

In sum, the combined teachings of Fortier and Galin do not suggest how to improve Fortier's hydrogel or how to arrive at the claimed subject matter with a reasonable expectation of success. Therefore, they cannot render the claims obvious because there is insufficient motivation to combine these references.

#### Response to Examiner's Comments

Page 6 – Examiner states that Galin shows that diisocyanate and PEG react via its urea groups. It is then concluded that this PEG would inherently involve binding of NCO to OH of PEG exposing NCO residues.

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First, Galin states that these groups are blocked. Therefore, as disclosed in Galin the modified PEG cannot reasonably be interpreted as being *inherently* capable of providing an albumin-free protein-hydrogel.

Second, the relevant inventive property in the claims is not merely having exposed NCO groups. A key property of the claimed hydrogel is having an activated PEG matrix that permits crosslinking to proteins so that the hydrogel does not dissolve in the absence of crosslinked albumin.

In addition, it is also important that the combined disclosures of Fortier and Galen provide no guidance that would allow one to predict that these hydrogels would not dissolve in the absence of albumin.

Continuing Page 6 to Page 7 -- Examiner states that Fortier's hydrogels are unstable and thus, that new improved hydrogel/enzyme crosslinking methods should be *attempted*, and that such *attempts* obviously include changing chemical structures of activators. She concludes that it would be obvious to link proteins, etc.

But the issue that Examiner continues to ignore is that the crosslinked proteins

- a) must retain catalytic activity, and
- b) are able to crosslink to a hydrogel in the absence of albumin; and
- c) without dissolving the hydrogel.

Not Fortier, Galin or Gould indicates that this should be expected, especially in view of the Fortier's failure. Focusing on Gould and Galin to provide evidence that PEG's may be reacted with polyglycols does nothing to create the expectation that the claimed protein-hydrogel would be obtained.

Page 8 – Examiner states that it is not necessary for Galin and Gould to be enabling, because they are only cited to show that PEG can be reacted with diisocyanates.

This statement is completely incorrect and runs counter to the law relating to virtually all prior art rejections. All references in 103 rejections, taken together, must provide an enabling disclosure.

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It is well established that a proper reference under 35 USC §§102 or 103 must be enabling in the sense of 35 USC §112, 1st paragraph. Pertinent is the following quote from *In re Le Grice*, 133 USPQ 365, 374 (CCPA 1962):

[T]he proper test of a description in a publication as a bar to a patent as the clause is used in section 102(b) requires a determination of whether one skilled in the art to which the invention pertains *could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination be put in possession of the invention* on which a patent is sought. [Emphasis added.]


See also, *In re Hoeksema*, 158 USPQ 596, 601 (CCPA 1968), wherein the Court stated:

While *In re Le Grice* was bottomed on an issue arising under 35 U.S.C. 102 where the reference was a printed publication, that test, in our view, is also properly applicable to issues arising under 35 U.S.C. 103.

The test for enablement for a reference, thus, is whether the prior art references describe all sources and methodology in such detail that a person of ordinary skill in the art could reproduce the results reported therein with a reasonable expectation of success. Clearly, Fortier combined with Galin are inadequate to satisfy this test. Consequently, these references are not properly relied upon to support the rejections, and therefore, the rejections should be withdrawn.

Respectfully Submitted,

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